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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/763,502	01/22/2004	Peter H. St. George-Hyslop	003237-0010-102	8497

7590 03/15/2007
James F. Haley, Jr
Fish & Neave IP Group
ROPES & GRAY LLP
1251 Avenue of the Americas
New York, NY 10020-1105

EXAMINER

CARLSON, KAREN C

ART UNIT	PAPER NUMBER
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1656

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/15/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/763,502

Applicant(s)

ST. GEORGE-HYSLOP ET AL.

Examiner

Karen Cochrane Carlson, Ph.D.

Art Unit

1656

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 January 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 and 3-6 is/are rejected.
- 7) ☒ Claim(s) 2 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>1/22/2004</u> . | 6) <input type="checkbox"/> Other: _____ |

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Applicant's election without traverse of Group 1, Claims 1-6, in the reply filed on January 9, 2007 is acknowledged.

Claims 7-33 have been cancelled. Claims 1-6 are currently pending and are under examination.

Benefit of priority is to April 1, 1999.

The disclosure is objected to because of the following informalities:

The priority information at page 1 needs to be updated to include the issued patents.

Appropriate correction is required.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 4-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In Claim 1, there is no function assigned to the "functional fragment" of PAMP.

Claim 4 refers to a mutant PAMP, for which there is no antecedent basis in Claim 1.

Applicants may wish to make Claim 4 an independent claim.

In Claim 5, it is not clear what the biochemical changes similar to mutations in PS-1, Ps2, or beta- amyloid are.

In Claim 6, there is no reference sequence identification number for the mutations listed.

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The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 3, and 4 are rejected under 35 U.S.C. 102(a) as being anticipated by or being unpatentable under 35 U.S.C. 103(a) by The *C. elegans* Sequencing Consortium (December 11, 1998; Science 282:2012-2018; see the sequence alignment for SEQ ID NO: 12 attached thereto).

The Consortium teaches an amino acid sequence that shares 99.7% identity to SEQ ID NO: 12. At page 34, para. 1 of the instant specification, the specification teaches that this *C. elegans* homologue of PAMP is identical to the sequence disclosed by the Consortium. Therefore, the teachings of the Consortium anticipate or render obvious the instant SEQ ID NO: 12 (Claim 1, 3). Claim 4 is included in this rejection because one PAMP can be considered to be a mutant of the PAMP of another species; thus, the *C. elegans* PAMP is a mutant of the human, mouse, and *Drosophila* PAMP, for example. Additionally, the *C. elegans* PAMP would be considered to comprise a functional fragment of the human, mouse, and *Drosophila* PAMP, for example.

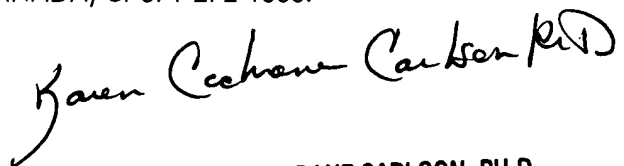
Claim 2 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Cochrane Carlson, Ph.D. whose telephone number is 571-272-0946. The examiner can normally be reached on 7:00 AM - 4:00 PM, off alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



KAREN COCHRANE CARLSON, PH.D.
PRIMARY EXAMINER

Attach to Science
282: 2012

SEQ ID NO: 12

```

<!--StartFragment-->RESULT 1
NICA_CAEEL
ID NICA_CAEEL STANDARD; PRT; 723 AA.
AC Q23316;
DT 15-JUL-1998, integrated into UniProtKB/Swiss-Prot.
DT 26-SEP-2003, sequence version 3.
DT 18-APR-2006, entry version 42.
DE Nicastrin precursor (Anterior-pharynx-defective protein 2).
GN Name=aph-2; ORFNames=ZC434.6;
OS Caenorhabditis elegans.
OC Eukaryota; Metazoa; Nematoda; Chromadorea; Rhabditida; Rhabditoidea;
OC Rhabditidae; Peloderinae; Caenorhabditis.
OX NCBI_TaxID=6239;
RN [1]
RP NUCLEOTIDE SEQUENCE [LARGE SCALE GENOMIC DNA].
RC STRAIN=Bristol N2;
RX MEDLINE=99069613; PubMed=9851916; DOI=10.1126/science.282.5396.2012;
RG The C. elegans sequencing consortium;
RT "Genome sequence of the nematode C. elegans: a platform for
RT investigating biology.";
RL Science 282:2012-2018(1998).
RN [2]
RP SEQUENCE REVISION.
RG WormBase consortium;
RL Submitted (JUN-2003) to the EMBL/GenBank/DDBJ databases.
RN [3]
RP FUNCTION, AND GENE NAME.
RX MEDLINE=20445163; PubMed=10993067; DOI=10.1038/35024009;
RA Yu G., Nishimura M., Arawaka S., Levitan D., Zhang L., Tandon A.,
RA Song Y.-Q., Rogaeva E., Chen F., Kawarai T., Supala A., Levesque L.,
RA Yu H., Yang D.-S., Holmes E., Milman P., Liang Y., Zhang D.M.,
RA Xu D.H., Sato C., Rogaev E., Smith M., Janus C., Zhang Y.,
RA Aebersold R., Farrer L.S., Sorbi S., Bruni A., Fraser P.E.,
RA St George-Hyslop P.H.;
RT "Nicastrin modulates presenilin-mediated notch/glp-1 signal
RT transduction and betaAPP processing.";
RL Nature 407:48-54(2000).
RN [4]
RP FUNCTION.
RX MEDLINE=20265922; PubMed=10804188;
RA Goutte C., Hepler W., Mickey K.M., Priess J.R.;
RT "aph-2 encodes a novel extracellular protein required for GLP-1-
RT mediated signaling.";
RL Development 127:2481-2492(2000).
CC -!- FUNCTION: Essential subunit of the gamma-secretase complex, an
CC endoprotease complex that catalyzes the intramembrane cleavage of
CC integral membrane proteins such as Notch (glp-1 or lin-12). It may
CC represents a stabilizing cofactor required for the assembly of the
CC gamma-secretase complex.
CC -!- SUBUNIT: Component of the gamma-secretase complex, a complex
CC probably composed of the presenilin homodimer (sel-12, hop-1 or
CC spe-4), nicastrin (aph-2), aph-1 and pen-2 (Probable).
CC -!- SUBCELLULAR LOCATION: Membrane; single-pass type I membrane
CC protein (Potential).
CC -!- SIMILARITY: Belongs to the nicastrin family.
CC -----
CC Copyrighted by the UniProt Consortium, see http://www.uniprot.org/terms
CC Distributed under the Creative Commons Attribution-NoDerivs License
CC -----
DR EMBL; Z75714; CAB00063.2; -; Genomic_DNA.
DR PIR; T27570; T27570.
DR UniGene; Cel.5001; -.
DR Ensembl; ZC434.6; Caenorhabditis elegans.
DR WormBase; WBGene00000148; aph-2.
DR WormPep; ZC434.6; CE15229.
DR InterPro; IPR008710; Nicastrin.
DR Pfam; PF05450; Nicastrin; 1.
KW Complete proteome; Glycoprotein; Membrane; Notch signaling pathway;
KW Signal; Transmembrane.
FT SIGNAL 1 16 Potential.
FT CHAIN 17 723 Nicastrin.
FT /FTId=PRO_0000019684..
FT TOPO_DOM 17 678 Extracellular (Potential).
FT TRANSMEM 679 699 Potential.
FT TOPO_DOM 700 723 Cytoplasmic (Potential).
FT CARBOHYD 40 40 N-linked (GlcNAc...) (Potential).

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FT CARBOHYD 181 181 N-linked (GlcNAc . .) (Potential).
 FT CARBOHYD 271 271 N-linked (GlcNAc . .) (Potential).
 FT CARBOHYD 328 328 N-linked (GlcNAc . .) (Potential).
 FT CARBOHYD 409 409 N-linked (GlcNAc . .) (Potential).
 FT CARBOHYD 627 627 N-linked (GlcNAc . .) (Potential).
 SQ SEQUENCE 723 AA; 81659 MW; C7DF2D12ADBFB8D9D CRC64;

Query Match 99.7%; Score 3789; DB 1; Length 723;
 Best Local Similarity 99.7%; Pred. No. 7.1e-264;
 Matches 721; Conservative 0; Mismatches 0; Indels 2; Gaps 1;

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Db    301 SVLTSIIISVLAAARSMGTQIEKWQKASNTSNRNVFFAFFNGESLDYIGSGAAAYQMENGK 360

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Db    481 EWTEDEREKAIQEIEAVSTAILAAAADYVGVETDEVVAKVDKKLITTFDCLITSNFWFD 540

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Qy    719 EPL 721
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Db    721 EPL 723

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<!--EndFragment-->